Essay

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Regulation of the pharmaceutical industry: promoting health or protecting wealth?

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Government has long had conflicting aims with regard to regulating the pharmaceutical industry. It is essential to control expenditure on pharmaceutical products, which in the UK currently exceeds £12 billion and consumes around 12% of the NHS budget.[1] In a time of static NHS funding, the opportunity costs of pharmaceuticals are all too clear. On the other hand, the government wants to protect the industry, encouraging investment, innovation, exports and economic growth. Public intervention in this private industry is essential, given the need to incentivise innovation through patents, which inevitably create monopolies that need further regulation. The Department of Health struggles to balance its role as both regulator and sponsor of the pharmaceutical industry, and there is a persistent risk of 'regulatory capture', where 'regulation is acquired by the industry and is designed and operated primarily for its benefit'.[2]

Over recent years, the global pharmaceutical industry has been challenged by economic recession and financial austerity. Healthcare, and high-cost pharmaceuticals in particular, are at national level a 'luxury good', which means that as economies grow they invest proportionally more in healthcare, but in economic hard times these budgets are a target for constraint.

Companies strive to maintain demand for their products in challenging times and also to reduce their own costs. Industry efforts to maintain demand have been varied and creative, including 'me-too drugs',[3] paying generic manufacturers to delay market entry[4] and even using safety systems for high-risk products as ways of delaying competition.[5]

Cost-control efforts include migration of research and development functions away from high-cost countries like the UK, particularly to India and China. The science base in these countries is developing rapidly, with large supplies of excellent chemists and biologists. With relatively low wages and large populations, the cost of clinical trials is also lower. The UK government is anxious to retain and enhance our domestic science base, incentivising investment from domestic and overseas companies by using a variety of policies of explicit and covert industry subsidies.

One element of this has been to undermine the National Institute for Health and Care Excellence. NICE, established in 1999 to evaluate rigorously new drugs and identify their clinical and cost effectiveness, has long been the target of industry hostility. Companies are required to present data including information on costs and quality of life and to demonstrate a cost-QALY ratio of generally less than £30,000 (where a QALY is one year of good quality life). In 2009, NICE was instructed to increase this threshold for end-of-life products, such as cancer drugs. Firms are free to set prices provided they do not exceed regulated rates of return on historical capital set out in successive Pharmaceutical Price Regulation Scheme (PPRS) agreements since 1957. If a product is shown to produce a QALY for an acceptable cost, NICE approves it for use in the NHS and commissioners are obliged to fund it. This system is inflationary and has added billions to NHS costs since 1999, partly because the cost-per-QALY threshold is relatively high, contentious and is not evidence-based. Recent empirical work commissioned by the Department of Health suggested that a threshold of less than £13,000 would be appropriate,[6] a suggestion which was greeted by industry with predictably loud opposition. Consequently, government instead agreed a new PPRS in December 2013 which guaranteed industry a cost-per-QALY cut-off 'at a level consistent with the current range' until 2018.[7]

There is now further pressure to ease the NICE cut-off and make it easier for products to obtain NHS reimbursement. This has been encouraged not only by industry but also by media, patient charities and politicians, although these groups may often be influenced, directly or indirectly, by industry funding. Not content with retaining the £30,000 cut-off, industry and others have lobbied for the widening of the

definitions of cost and effect used by NICE. NICE currently uses an NHS perspective, with cost estimates based on NHS resource use alongside effects measured in terms of improved length and quality of life for patients. Some drugs may reduce the costs and improve the quality of life of others in society, e.g. carers. Broadening the scope of cost and effect definitions to include 'wider societal impact'[8] is again potentially inflationary as more drugs may be approved by NICE.

The Coalition government has also renewed and increased the Cancer Drugs Fund, which allocates £280 million per year to non-NICE approved cancer drugs on a case-by-case basis. Roche, the leading manufacturer of cancer drugs, is the major beneficiary. This policy served two political goals: the garnering of votes from public interest groups focused on cancer and the subsidisation of the pharmaceutical industry. Products like ado-trastuzumab emtansine (Kadcyla), rejected by NICE due to cost (£90,000 for a course of treatment, translating to £166,000 per QALY) can be funded individually, reducing the downward pressure on high-cost drugs.[9] This is an inequitable and inefficient scheme. It is inefficient because pharmaceuticals are financed regardless of whether they meet an appropriate cost-QALY threshold, subverting NICE processes. It is inequitable because it discriminates against other diseases which may be equally in need of additional funding.

In March 2014, the government announced further help for the industry. The search for new chemical entities which improve patient health is very costly mainly due to many potentially viable substances failing in the development process.[10] The regulatory system requires that products meet safety, efficacy and quality controls, although often there is incomplete reporting of trials to regulators.[11] Despite this, a new scheme is to be introduced to fast track drugs for severely ill patients, allowing them to gain access to drugs still in development.[12] A company that can demonstrate safety and potential patient benefit to the Medicines and Health Care Regulator will be able to market the product, while bearing the cost and collecting data for product promotion worldwide when a full product licence is acquired. The announcement of this scheme was accompanied by Ministerial statements saying this would enhance the science base in the UK in the face of strong competition.

These policies are supporting pharmaceutical science and enhancing export income, but at a considerable opportunity cost to the NHS. One example is the treatment of age-related macular degeneration, a condition which impairs and removes sight. Genentech has developed two very similar products for different conditions: bevacizumab (Avastin) for the treatment of colorectal cancer and ranibizumab (Lucentis) for the treatment of macular degeneration. Both products were developed by Genentech, and one was licenced to Roche and one to Novartis. As Roche now owns Genentech, it receives royalties from Novartis and so has a commercial interest in both products.[13] Ranibizumab is marketed at over 10 times the price of bevacizumab, and clinical trials have shown equivalent efficacy in the treatment of macular degeneration.[14,15] A systematic review of safety found no detectable difference between the two products in relation to death or all serious systemic adverse events.[16] In the NHS and much of Europe, there are numerous legal and regulatory hurdles to using bevacizumab for macular degeneration, as it has a product licence only for use in cancer.[17] Switching patients in England to bevacizumab could in principle save the NHS over £100 million each year,[18] but Roche and Novartis challenge legally commissioners who seek greater efficiency in the use of their constrained budgets in this way. Under patent legislation and due to PPRS price freedom, government is powerless, or quietly condones excessive pricing as a means of supporting companies. As a consequence profits are inflated at the cost of NHS patient care. In Italy, a recent legal challenge from the country's anti-trust agency resulted in a fine of €182.5 million to Roche and Novartis for cartel behaviour, collusion to exclude the use of the cheaper drug and channel demand towards the more expensive.[14]

In general, UK drug prices are lower than those in the USA and some other countries, but higher than many other countries and perhaps higher than they need to be because of successive governments' desire to support the pharmaceutical science base and exports. The costs and benefits of these policies lack transparency and are inconsistent with evidence-based policy. A recent large systematic review of interventions to control pharmaceutical expenditure around the world found that although evidence for interventions influencing patients and prescribers has developed over recent years, evidence guiding regulation of industry is almost non-existent.[18] The market for pharmaceuticals is characterised by extensive, *ad hoc* regulatory reforms which often lack evidence and may be inconsistent with competing policy objectives of regulators.

The myriad of regulations affecting pharmaceutical innovation, production and marketing creates a regulatory jungle with net benefits that remain unclear despite decades of analysis, criticism and reform efforts.[19,20] Regulation of this expensive market is essential but this should be based on clear

objectives and robust evaluation of its costs and benefits. Government continues to subvert the efficiency of technology appraisal work carried out by NICE in order to subsidise industry. Does this benefit the UK taxpayer and NHS patients? Or does government tacitly wish to tax the NHS with high pharmaceutical prices of sometimes inefficient drugs and, in so doing, increase the wealth of industry? Current policy lacks accountability and appears consistent with Stigler's contention that regulation benefits the regulated.

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